

## REMARKS

### Support for the Amendments

Claims 1 and 2 have been amended to correct a typographical error and to exclude a specific compound disclosed in the specification, for example, at page 41, line 1 to page 42, line 11, based on M.P.E.P. § 2173.05(i).

### The Office Action

Claims 1-24 are pending. Claims 1-3, 6-9, 11, 12, 14, 15, and 18-24 are under consideration. Claims 4, 5, and 13 are drawn to a nonelected species. Claims 1-3, 6-9, 11, 12, 14, 15, and 18-24 stand rejected for obviousness over Klunk et al. (U.S. Patent No. 6,417,178; hereafter “Klunk 1”) in view of Klunk et al. (Life Sciences 1998 63:1807-1814; hereafter “Klunk 2”) and Huang et al. (Somatic Cell and Molecular Genetics 1998 24:217-233; hereafter “Huang”).

### Rejections under 35 U.S.C. § 103(a)

Claims 1-3, 6-9, 11, 12, 14, 15, and 18-24 stand rejected for obviousness over Klunk 1 in view of Klunk 2 and Huang. We note that claim 11 is not directed to the elected species. Independent claims 1 and 2, from which all other rejected claims depend, are directed to methods of decreasing cell death or toxicity or decreasing aggregate or inclusion formation as a result of expanded polyglutamine repeats by administering Congo red (diphenyldiazo-bis-alpha-naphthylaminesulfonate) or a pharmaceutically

effective derivative. An exemplary disease caused by expanded polyglutamine repeats is Huntington's disease. Applicants traverse this rejection.

To support an obviousness rejection, the Office must put forth a *prima facie* case that meets the legal standard for obviousness found in M.P.E.P. § 2142, which states:

To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success.

Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not based on applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 U.S.P.Q. 2d 1438 (Fed. Cir. 1991) (emphasis added).

In addition, as the Federal Circuit recently observed:

A critical step in analyzing the patentability of claims pursuant to section 103(a) is casting the mind back to the time of invention, to consider the thinking of one of ordinary skill in the art, guided only by the prior art references and the then-accepted wisdom in the field. . . . Most if not all inventions arise from a combination of old elements. . . . Thus, every element of a claimed invention may often be found in the prior art. . . . However, identification in the prior art of each individual part claimed is insufficient to defeat patentability of the whole claimed invention. . . . Rather, to establish obviousness based on a combination of the elements disclosed in the prior art, there must be some motivation, suggestion or teaching of the desirability of making the specific combination that was made by the applicant. *In re Kotzab*, 217 F.3d 1365, 1369-70, 55 U.S.P.Q.2d 1313, 1316 (Fed. Cir. 2000) (citations omitted) (emphasis added).

The evidence of a suggestion, teaching, or motivation to combine "must be clear and particular." *Dembiczak*, 175 F.3d at 999, 50 U.S.P.Q.2d at 1617. "Defining the problem in terms of its solution reveals improper hindsight in the selection of the prior art relevant

to obviousness.” *Monarch Knitting Mach. Corp. v. Sulzer Morat GMBH*, 139 F.3d 877, 881, 45 U.S.P.Q.2d 1977, 1981 (Fed. Cir. 1998). “Broad conclusory statements regarding the teaching of multiple references, standing alone, are not ‘evidence.’” *Dembiczak*, 175 F.3d at 999, 50 U.S.P.Q.2d at 1617.

In the present case, the Office has identified the elements of Congo red and treatment of Huntington’s disease separately in the prior art, but this alone is insufficient to negate patentability. The Federal Circuit further requires an Examiner to show a motivation to combine the references that create the case of obviousness to avoid hindsight based on the invention to defeat patentability of the invention. *In re Rouffet*, 149 F.3d 1350, 1357, 47 U.S.P.Q.2d 1453, 1457 (Fed. Cir. 1998). That is, “the examiner must show reasons that the skilled artisan, confronted with the same problems as the inventor and with no knowledge of the claimed invention, would select the elements from the cited prior art references for combination in the manner claimed.” *Id.* (emphasis added). Therefore, the Office must provide reasons from the prior art why one skilled in the art would employ Congo red in a method for treating conditions associated with polyglutamine repeats, as required in the instant claims. Furthermore, “the factual question of motivation [to combine references] is material to patentability, and ...[cannot] be resolved on subjective belief and unknown authority.” *Lee*, 277 F.3d at 1344, 61 U.S.P.Q.2d at 1434. Rather, the motivation to combine references “must be based on objective evidence of record.” *Lee*, 277 F.3d at 1343, 61 U.S.P.Q.2d at 1433. Thus, the

Office's reasoning must be based on documentary evidence disclosing a motivation to employ Congo red in the claimed methods in order to support an obviousness rejection.

Applicants assert that the Office has failed to establish a *prima facie* case of obviousness in the present case as the cited references fail to provide motivation to combine or modify the references, and there is no reasonable expectation of success.

*There is no motivation to combine or modify the cited references.*

The Office has cited the combination of three references as rendering claims 1-3, 6-9, 11, 12, 14, 15, and 18-24 obvious. In making this rejection, the Office acknowledges that neither Klunk 1 nor Klunk 2 provides a motivation to employ Congo red as a treatment for Huntington's disease (page 3), relying on Huang to remedy this deficiency. Applicants, however, assert that each of the cited references actually teaches away from the instant invention and, thus, fails to provide the necessary motivation.

Klunk 1 teaches that specific derivatives of Chrysamine G are useful for treating amyloid diseases. Applicants note that the instant claims have been amended to exclude Chrysamine G, a non-working embodiment of the instant invention. Regarding Congo red, Klunk 1 states, “[Prior art] data indicate that amyloid-binding compounds such as Chrysamine G and its derivatives, which are similar to Congo red but which, unlike Congo red, enter the brain well, would be effective in preventing cell degeneration and toxicity associated with fibril formation in amyloidosis associated conditions.” (Col. 25, ll. 2-7) (emphasis added) Thus, Klunk 1 explicitly teaches that Congo red is undesirable

as a therapeutic agent, and, based on this disclosure, one skilled in the art would not be motivated to employ Congo red in a treatment for a neurological disorder cause by expanded polyglutamine repeats, as instantly claimed.

The term “Huntington’s disease” is, furthermore, used only once, in claim 18, in Klunk 1. Claim 18 depends from claim 15, which, while providing formulae that cover numerous potential therapeutic compounds, does not cover Congo red. Thus, in addition to the explicit teaching of the unsuitability of Congo red as a treatment for neurological disease in general, Klunk 1 fails to provide any connection between Huntington’s disease and treatment of the same with Congo red.

With regard to Klunk 2, the Office relies on the abstract to provide motivation for employing Congo red in a treatment method, stating “Klunk [2] teaches that Congo red and the Congo red analogues employed in [Klunk 1] are known to be similarly useful as amyloid binding agents for reducing toxicity. See, the abstract.” This statement is incorrect as the only analog of Congo red disclosed by Klunk 2 is Chrysamine G, which as stated above is excluded in the instant claims. In addition, the Office’s position ignores the very next sentence in the abstract, which states, “Since Congo red is too highly charged to enter the brain in significant quantities, a lipophilic derivative, Chrysamine G, was tested...” (emphasis added) Thus, like Klunk 1, Klunk 2 clearly teaches away from the use of Congo red as a treatment for expanded polyglutamine repeats, as instantly claimed.

Applicants further note that the instant invention is directed to the treatment of expanded polyglutamine repeats and not A $\beta$  diseases. Thus, teachings of Klunk 2 regarding the utility vel non of Congo red for treating A $\beta$  diseases are irrelevant to the patentability of the instant claims.

As stated above, the Office relies on Huang to provide motivation for employing Congo red in a treatment for Huntington's disease stating, “[The abstract of] Huang et al. teaches that Congo red binding to the amyloid from Huntington diseases which have expanded polyglutamine segment.” First, Applicants direct the Office's attention to M.P.E.P. § 706.02, which states:

Citation of and reliance upon an abstract without citation of and reliance upon the underlying scientific document is generally inappropriate where both the abstract and the underlying document are prior art. See *Ex parte Jones*, 62 USPQ2d 1206, 1208 (Bd. Pat. App. & Inter. 2001) (unpublished).... It is not uncommon for a full text document to reveal that the document fully anticipates an invention that the abstract renders obvious at best. The converse may also be true, that the full text document will include teachings away from the invention that will preclude an obviousness rejection under 35 U.S.C. 103, when the abstract alone appears to support the rejection. (emphasis added)

In this case, the full text of Huang, a copy of which is enclosed, also teaches away from the instant invention. Huang states, “Interestingly, Congo red staining has not proved valuable for visualizing intraneuronal inclusions in HD brain, suggesting that the *in vivo* huntingtin aggregates have a complexity greater than the amyloid deposits seen in other disorders.” (pg. 229, col. 1) (emphasis added). The inability of Congo red to stain *in vivo* aggregates, i.e., those actually occurring in animals, teaches away from its utility as an *in*

*vivo* therapeutic agent, based on the Office's reasoning. Finally, while Congo red may stain huntingtin aggregates under some circumstances, the Office has failed to provide any documentary evidence why this occurrence would lead one skilled in the art to employ Congo red in a treatment for Huntington's disease, and, in the absence of such evidence, the rejection may not be maintained (M.P.E.P. § 2144.03(c)).

Since each reference teaches away from the use of Congo red as a therapeutic compound, there is no motivation to combine or modify the cited references to provide the instant invention.

*There is no reasonable expectation of success.*

The prior art also fails to provide a reasonable expectation of success. As stated above, both Klunk 1 and Klunk 2 explicitly state that Congo red is unsuitable as a therapeutic agent because of its purported inability to enter the brain. Huang also does not provide a reasonable expectation of success for the instant invention, because as discussed above, Huang teaches that Congo red is ineffective as a stain for *in vivo* huntingtin aggregates. Thus, the references teach that Congo red is unsuitable for therapeutic use, and the prior art cannot provide a reasonable expectation of success, as required by law.

In sum, none of the cited references provides a motivation to combine or modify the reference teachings, and, based on these references, there is no reasonable expectation

of success. Accordingly, the rejection of claims 1-3, 6-9, 11, 12, 14, 15, and 18-24 for obviousness should be withdrawn.

### CONCLUSION

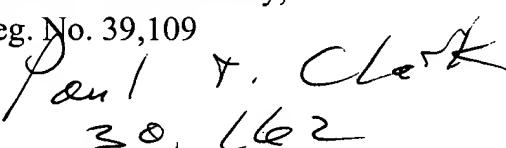
Applicants submit that the claims are in condition for allowance, and such action is respectfully requested. Enclosed is a Petition to extend the period for replying for three months, to and including December 13, 2003, and a check in payment of the required extension fee. If there are any additional charges or any credits, please apply them to Deposit Account No. 03-2095.

Respectfully submitted,

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